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Verification of a semi-automated MRI-guided technique for non-invasive determination of the arterial input function in ^{15}O-labeled gaseous PET

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ABSTRACT

A semi-automated MR-guided technique has been evaluated for non-invasive estimation of cerebral metabolic rate of oxygen ($CMRO_2$) using the sequential administration of ^{15}O oxygen (O_2) and ^{15}O carbon dioxide (CO_2) during a single PET scan. Two mathematical models, which assess the arterial input function (AIF) from time-activity curves (TAC) in the internal carotid artery region, were tested, namely one with a simple correction for the recovery coefficient (RC) and another with corrections for RC and spillover from surrounding tissues. RC was determined from MRA and black-blood image. RC was also determined from $C^{15}O$ blood volume images as a reference. RC agreed between MR-based and $C^{15}O$-PET based methods, suggesting validity of MR-based methods. Area-under-the-curve (AUC) of the early portion of estimated AIF agreed with that of measured AIF in both models. AUC of the delayed phase of estimated AIF was largely overestimated in the first model, but was sufficiently improved by the spillover correction implemented in the second model.

1. Introduction

PET study using ^{15}O gases ($^{15}O_2$, $C^{15}O_2$, $C^{15}O$, and $H_2^{15}O$) provides absolute quantification of cerebral blood flow (CBF), cerebral metabolic rate of oxygen ($CMRO_2$), oxygen extraction fraction (OEF), and cerebral blood volume (CBV). The continuous monitoring of the arterial radioactivity concentration using a small detector is prerequisite, but has been considered non-practical for a clinical use due to its invasiveness and the need for labor intensive work. Recent advances in PET devices enable quantitative assessment of time–activity curves (TAC) in the area of the internal carotid artery (ICA), by which arterial input functions (AIF) may be replaced. However, the small structure of the ICA causes systematic underestimation due to small recovery coefficient (RC) and spillover (SP) from the surrounding tissues [1]. Hybrid MR/PET has a potential providing the PET-derive AIF with accurate and reliable corrections for RC and SP using MR-based anatomical information.

This study was intended to develop a semi-automated technique to derive AIF for a series of ^{15}O-PET scans using MR images. Validity of the technique is tested in the series of PET scans performed on healthy volunteers. The impact of RC and SP corrections has also been evaluated.

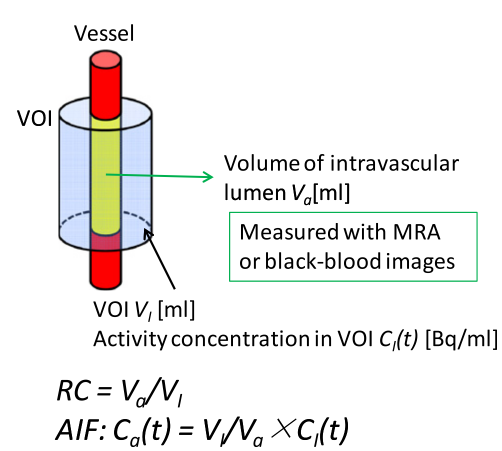

Fig. 1. Mathematical model for AIF estimation with a simple correction for the recovery coefficient (model-1).

Abbreviations: CBF, cerebral blood flow; $CMRO_2$, cerebral metabolic rate of oxygen; OEF, oxygen extraction fraction; CBV, cerebral blood volume; TAC, time-activity curve; ICA, internal carotid artery; AIF, arterial input function; RC, recovery coefficient; SP, spillover; VOI, volume-of-interest; DARG, dual-tracer autoradiographic method; TOF-MRA, time-of-flight magnetic resonance angiography; BB-FRFSE, black-blood fast recovery fast spin echo; AUC, area under the curve

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2. Method

2.1. Imaging protocol

Scans were carried out 9 times, on 7 healthy volunteers of 26+/−10 years old. The scanner was mCT from Siemens enabling 3D PET with adequate corrections for randoms, deadtime count loss, attenuation and scatter. Special attention was made in the scatter correction process to take into account for the strong radioactivity in gaseous form in the facemask. The scan protocol followed a recently proposed rapid dual-tracer autoradiographic method (DARG) [2,3], in which $^{15}O_2$ and $C^{15}O_2$ gases were inhaled sequentially within a 4.5 min interval, during a single PET scan over 9 min. A continuous arterial blood sampling was carried out, and AIF was assessed using a coincidence block detector, with adequate correction for delay and dispersion. Additional PET images were obtained with ^{15}O carbon monoxide (CO) inhalation to measure the RC of a volumes-of-interest (VOI) on ICA. Images were reconstructed at 5 sec interval, to which two VOIs were placed on the ICA region using semi-automated software. MR images were separately acquired on each volunteer with the sequence of 3D time-of-flight MR angiography (TOF-MRA) and 3D black-blood fast recovery fast spin echo (BB-FRFSE). The pixel size of the MR image was $0.6 \times 0.8 \times 1.0$ mm^3 for TOF-MRA and $0.4 \times 0.4 \times 2.0$ mm^3 for BB-FRFSE.

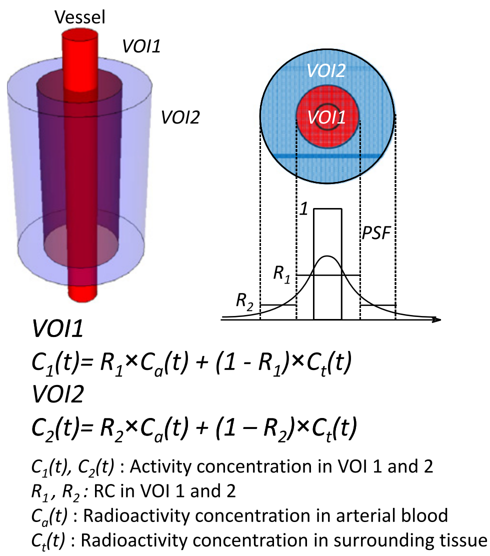

Fig. 2. Mathematical model for AIF estimation with recovery coefficient and spillover correction (model-2).

Table 1
Comparison of AUC in the early phase of O_2 and CO_2 inhalation with a simple correction for the recovery coefficient.

	AUC ratio for O_2 (0–60 sec)			AUC ratio for CO_2 (0–60 sec)		
Subject	TOF-MRA	BB-FRFSE	CO	TOF-MRA	BB-FRFSE	CO
001-1	0.88	0.91	0.92	0.89	0.92	0.92
002-1	1.15	1.22	1.21	1.12	1.18	1.21
003-1	1.41	1.14	1.13	1.29	1.05	1.13
004-1	1.06	0.96	1.02	1.13	1.02	1.02
005-1	1.15	1.04	1.03	1.20	1.09	1.03
006-1	1.17	1.11	1.07	1.22	1.16	1.07
006-2	1.32	1.25	1.22	1.33	1.26	1.22
007-1	0.92	0.87	0.95	1.01	0.96	0.95
007-2	1.11	1.05	1.11	0.96	0.91	1.11
Mean	1.13	1.06	1.07	1.13	1.06	1.07
SD	0.17	0.13	0.11	0.15	0.12	0.11

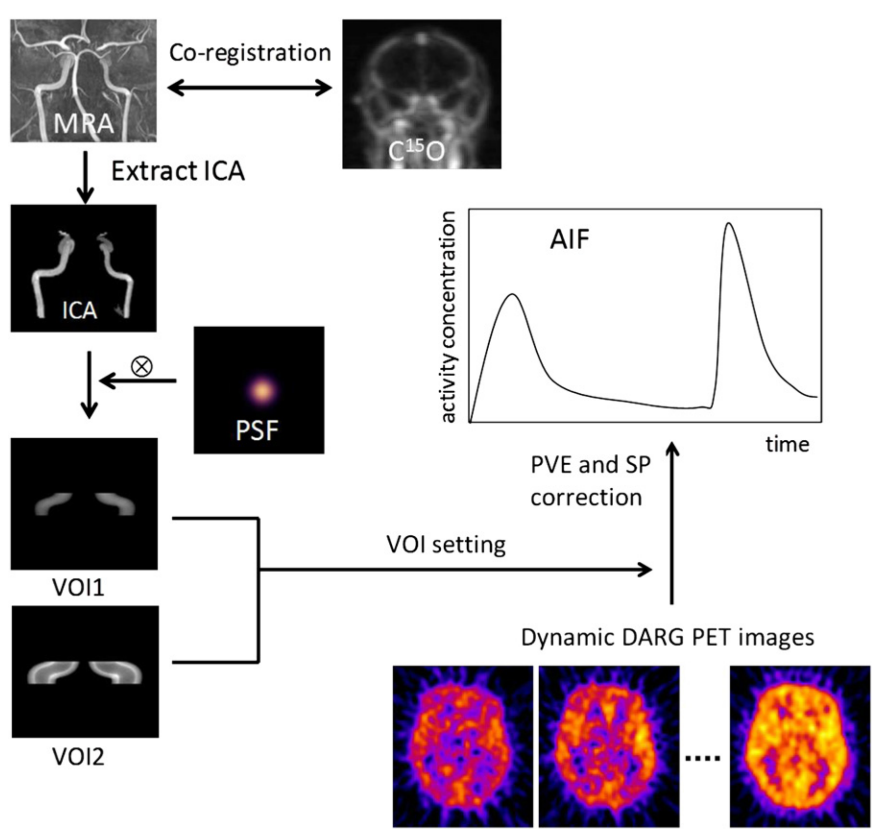

Fig. 3. Image processing for the AIF estimation by using semi-automated software. The process includes co-registration of MRI and PET images, automated extraction of ICA region, and calculation of AIF from dynamic PET images with RC and SP correction using two VOIs.

Table 2
Comparison of AUC in delayed phase of O_2 and CO_2 inhalation with a simple correction for the recovery coefficient.

	AUC ratio for O_2 (60–120 sec)			AUC ratio for CO_2 (60–120 sec)		
Subject	TOF-MRA	BB-FRFSE	CO	TOF-MRA	BB-FRFSE	CO
001-1	1.63	1.69	1.67	2.10	2.18	1.67
002-1	1.65	1.75	1.69	2.58	2.73	1.69
003-1	2.50	2.03	1.95	3.33	2.7	1.95
004-1	1.72	1.56	1.57	2.53	2.29	1.57
005-1	1.67	1.51	1.41	2.12	1.92	1.41
006-1	1.72	1.63	1.47	1.99	1.89	1.47
006-2	1.74	1.65	1.52	1.90	1.8	1.52
007-1	1.40	1.33	1.31	1.66	1.57	1.31
007-2	1.35	1.28	1.29	1.68	1.59	1.29
Mean	1.71	1.60	1.54	2.21	2.07	1.54
SD	0.33	0.22	0.21	0.53	0.43	0.21

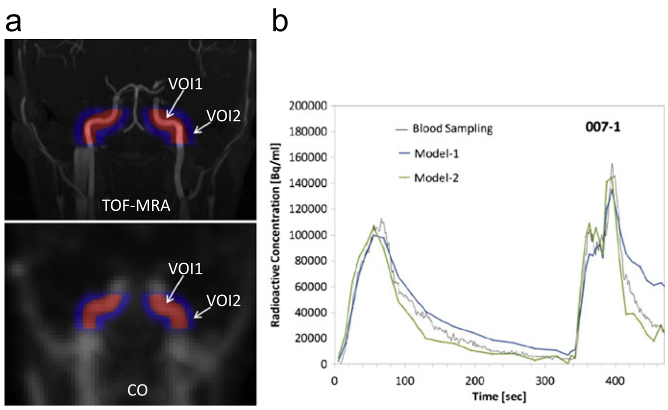

Fig. 4. a: Example of VOI setting fused on maximum projection images of TOF-MRA and CO PET data. VOI 1 and 2 were shown as red and blue region, respectively. b: Measured and estimated input functions in one subject. AIFs were estimated with the mathematical model-1 and model-2.

2.2. Model-1 (only RC correction)

To correct for the underestimation of the input function from ICA TAC, a mathematical model shown in Fig. 1 was applied to determine AIF with a correction for RC. The RC, which was defined as the volume of intravascular lumen-to-the volume of VOI ratio, was calculated using TOF-MRA and BB-FRFSE anatomical images, and was applied to ICA TAC to determine RC-corrected AIFs. RC was also determined from the $C^{15}O$ blood volume image in PET, and was applied to determine AIF.

2.3. Model-2 (RC and SP correction)

Correction for SP of radioactivity from surrounding tissues was taken into account, in addition to the RC correction described in the model-1. The mathematical model shown in Fig. 2 was used, and AIF was determined for given RC values for each of 2 VOIs. The process of image analysis for the AIF estimation using model-2 is shown in Fig. 3.

3. Results

The results of area under the curve (AUC) ratio for the three methods to determine RC for early portion (initial 60 sec) of $^{15}O_2$ and $C^{15}O_2$ scans obtained using the model-1 are summarized in Table 1. Similarly, the results for the delayed portion (60–120 sec) are summarized in Table 2. AIFs determined from ICA were 2.5–4.0 smaller than the measured AIFs. The simple correction for RC using TOF-MRA, BB-FRFSE, and CO images improved the agreement of AUC in the early part, but significantly overestimated in the delayed part.

Table 3
Comparison of AUC in early phase of O_2 and CO_2 inhalation with RC and SP correction.

	AUC ratio for O_2 (0–60 sec)		AUC ratio for CO_2 (0–60 sec)	
Subject	Model-1	Model-2	Model-1	Model-2
001-1	0.94	0.65	1.07	0.84
002-1	1.43	1.25	1.45	1.20
003-1	1.48	0.96	1.46	0.99
004-1	1.18	1.00	1.29	0.91
005-1	1.29	0.89	1.27	0.98
006-1	1.28	1.20	1.32	1.20
006-2	1.44	1.18	1.47	1.21
007-1	1.02	1.04	1.08	1.07
007-2	1.07	1.09	0.93	0.97
Mean	1.24	1.03	1.26	1.04
SD	0.20	0.18	0.20	0.14

Table 4
Comparison of AUC in delayed phase of O_2 and CO_2 inhalation with RC and SP correction.

	AUC ratio for O_2 (60–120 sec)		AUC ratio for CO_2 (60–120 sec)	
Subject	Model-1	Model-2	Model-1	Model-2
001-1	1.46	0.77	2.32	0.81
002-1	1.75	1.20	2.91	1.09
003-1	2.25	1.19	3.69	1.05
004-1	1.59	0.99	2.88	0.73
005-1	1.62	0.84	2.24	0.84
006-1	1.68	1.09	2.27	0.99
006-2	1.66	1.01	2.19	0.80
007-1	1.30	0.89	1.83	0.79
007-2	1.11	0.78	1.56	0.85
Mean	1.60	0.97	2.43	0.88
SD	0.32	0.17	0.64	0.13

Corrections for SP in addition to RC using the two VOIs (Fig. 4a) improved the agreement in AUC as compared with the invasive AIFs particularly for the delayed portion for both O_2 and CO_2 inhalation periods, as shown in Fig. 4b. The results of AUC comparison of model-1 and model-2 were summarized in Tables 3 and 4.

4. Conclusion

In the present study, we demonstrated the non-invasive MRI-guided AIF estimation from TAC in the ICA region in ^{15}O labeled gaseous PET. The AUC of the early phase of estimated AIF well agreed with that of measured AIF. On the other hand, The AUC of the delayed phase of estimated AIF was largely overestimated in model-1, and improved in model-2 by incorporating the SP correction with additional VOI placed surrounding area of the ICA.

These findings suggest that the combination of MR with ^{15}O gaseous PET enables a rapid and quantitative assessment of oxygen utilization simultaneously with the cerebral perfusion, providing unique opportunity for clinical research.

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